Application No.: 10/706791 Customer No. 25291
Inventors: Christopher William Aston et al.
Attorney Docket No.: AM101119
Title: METHODS AND COMPOSITIONS FOR TREATING....

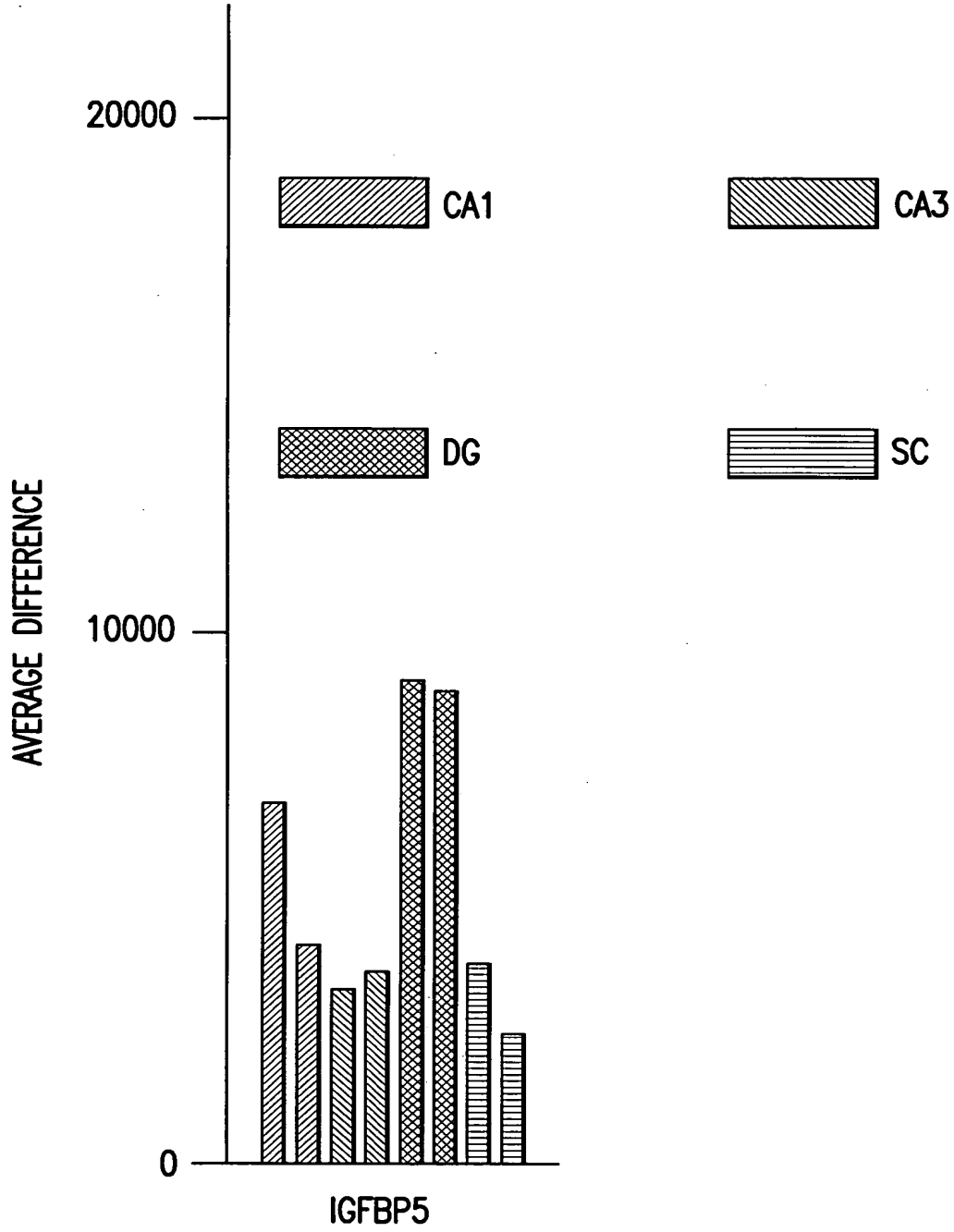

FIG. 1

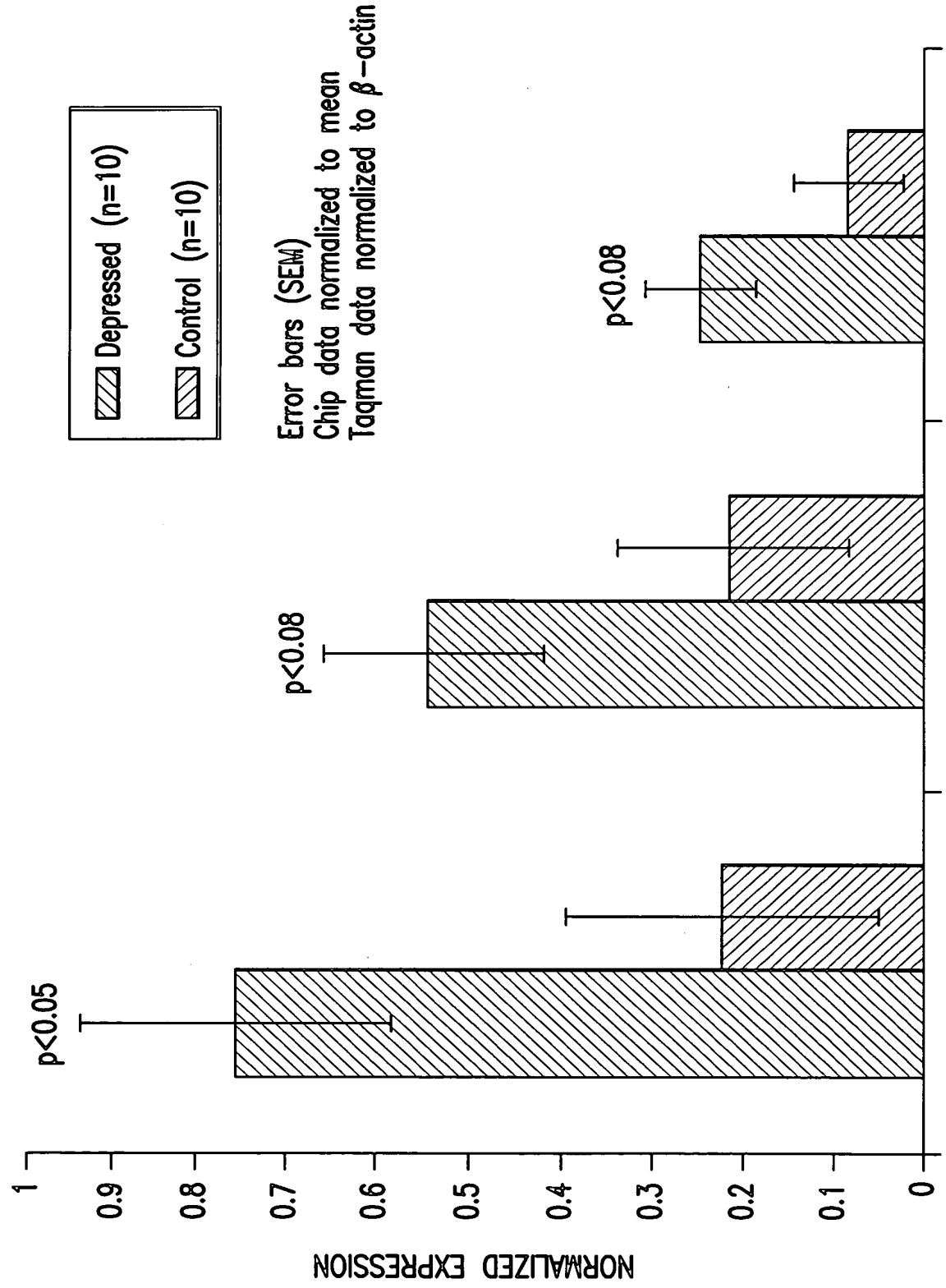
NORMALIZED EXPRESSION
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
p<0.05
p<0.08
p<0.08
GIHuman1A
HuGeneFL
Taqman
Depressed (n=10)
Control (n=10)
Error bars (SEM)
Chip data normalized to mean
Taqman data normalized to β-actin

FIG. 2

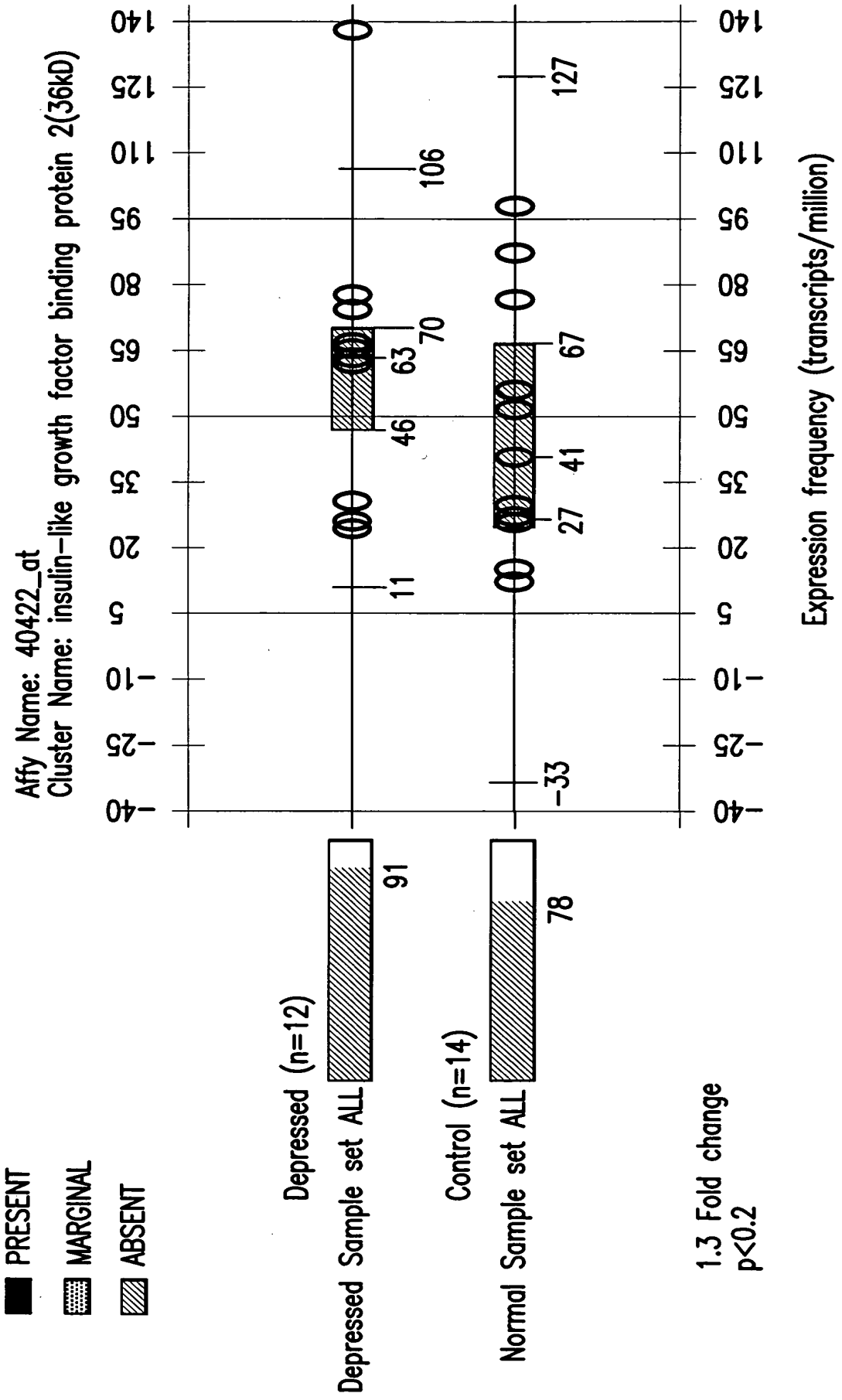
Affy Name: 40422_at
Cluster Name: insulin-like growth factor binding protein 2(36kD)
Expression frequency (transcripts/million)
140
125
110
95
80
65
50
35
20
5
-10
-25
-40
106
127
70
63
67
46
41
27
11
-33
PRESENT
MARGINAL
ABSENT
Depressed (n=12)
Depressed Sample set ALL
91
Control (n=14)
Normal Sample set ALL
78
1.3 Fold change
p<0.2

FIG.3

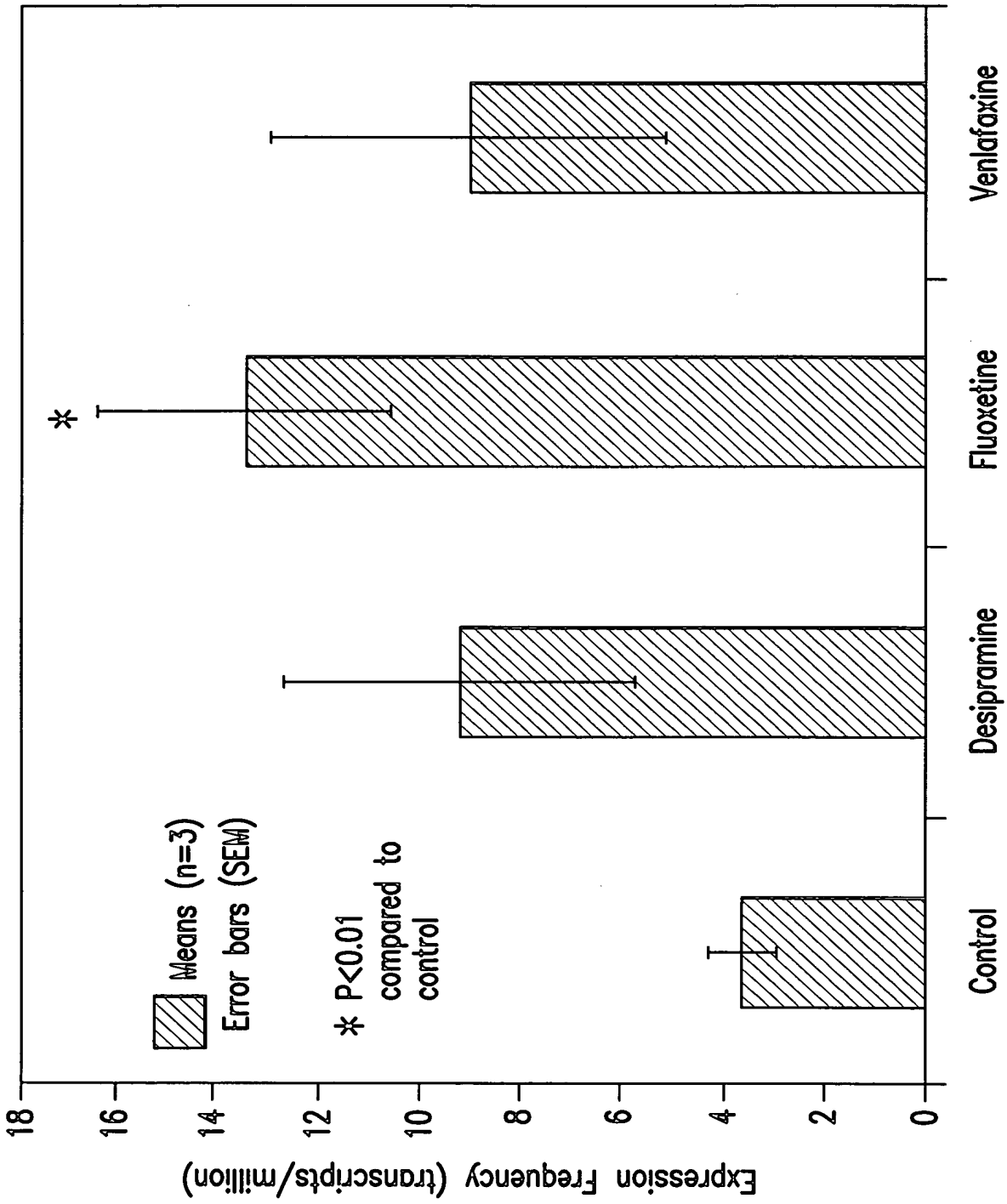
Expression Frequency (transcripts/million)
0
2
4
6
8
10
12
14
16
18
Means (n=3)
Error bars (SEM)
* P<0.01
compared to
control
*
Control
Desipramine
Fluoxetine
Venlafaxine

FIG. 4

Original gel spot #	Protein Identity	Function	Venlafaxine (Fold change)	Fluoxetine (Fold change)	Accession#	MOWSE score	Protein Area Coverage	Mr/pI	Species
87	IGF-1 A precursor	GH is an important regulator of IGF-1 expression. Secreted/Growth-promoting activity.	2.9	2.5	P08025	7.07E+01	28%	17079/ 9.5	Rat

FIG.5

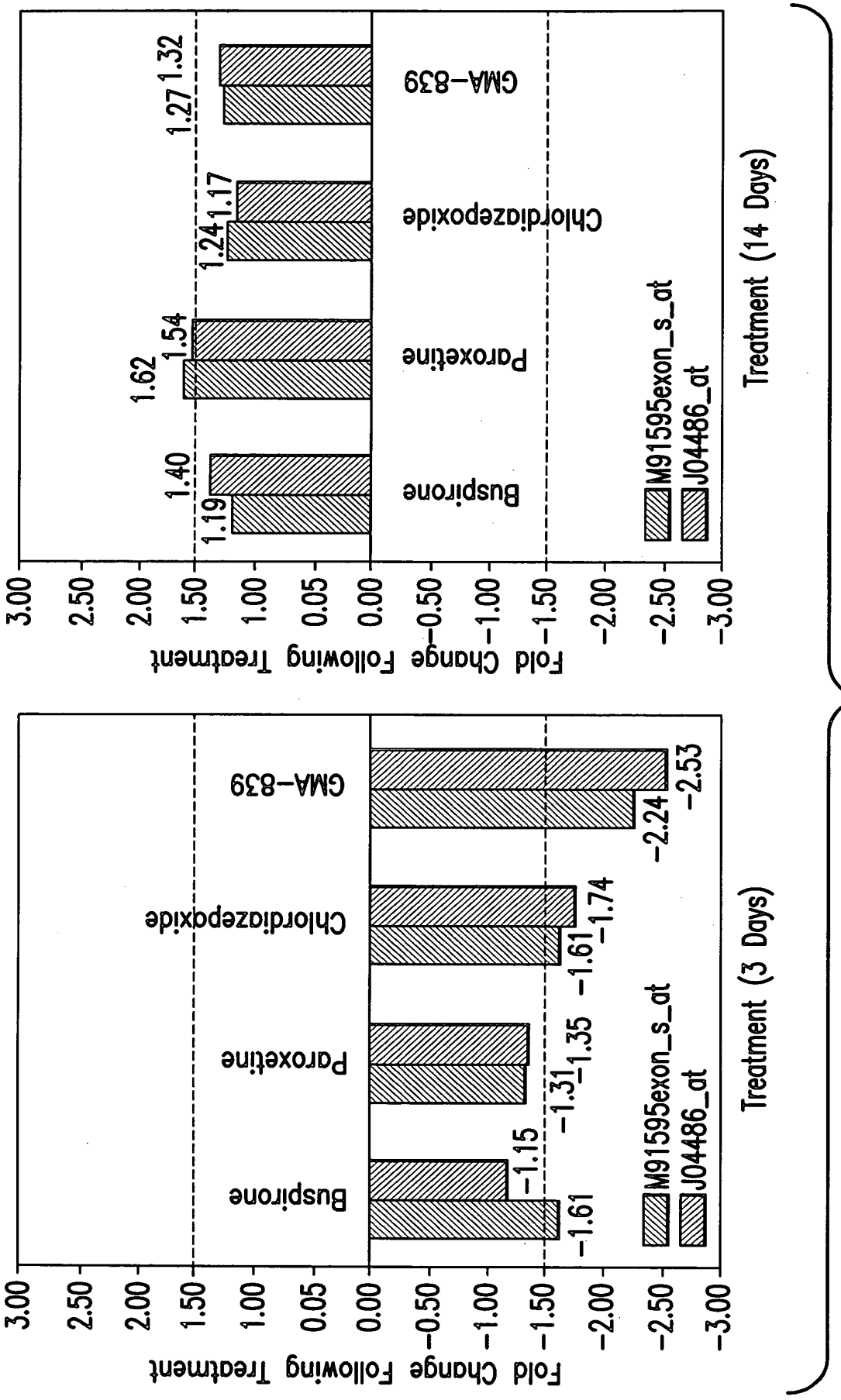
Fold Change Following Treatment
3.00
2.50
2.00
1.50
1.00
0.05
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
Buspirone
Paroxetine
Chlordiazepoxide
GMA-839
1.40
1.19
1.62
1.54
1.24
1.17
1.27
1.32
M91595exon_s_at
J04486_at
Treatment (14 Days)
Fold Change Following Treatment
Buspirone
Paroxetine
Chlordiazepoxide
GMA-839
-1.15
-1.61
-1.31
-1.35
-1.61
-1.74
-2.24
-2.53
M91595exon_s_at
J04486_at
Treatment (3 Days)

FIG. 6

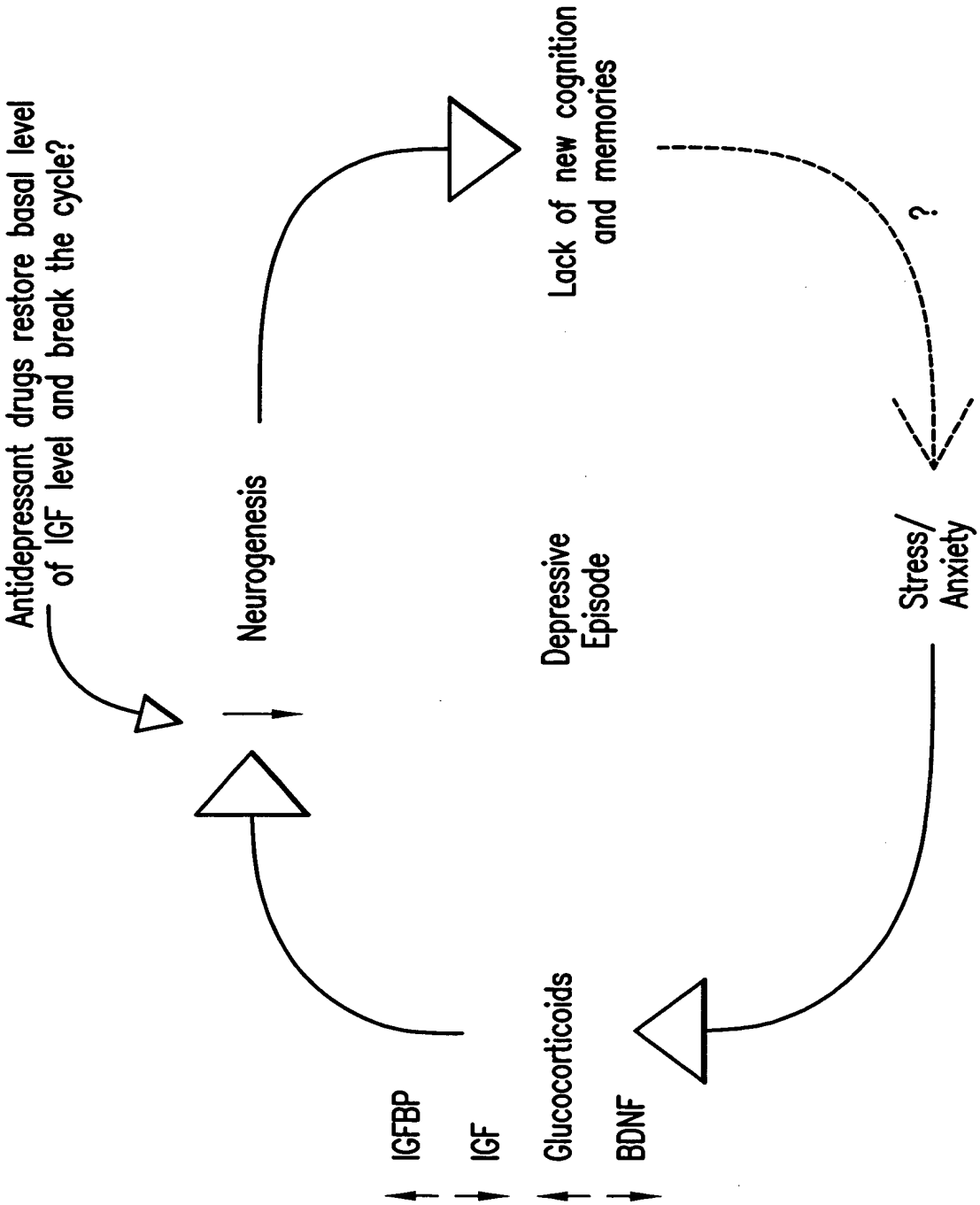
Antidepressant drugs restore basal level of IGF level and break the cycle?
Neurogenesis
Depressive Episode
Lack of new cognition and memories
?
Stress/ Anxiety
IGFBP
IGF
Glucocorticoids
BDNF

FIG. 7

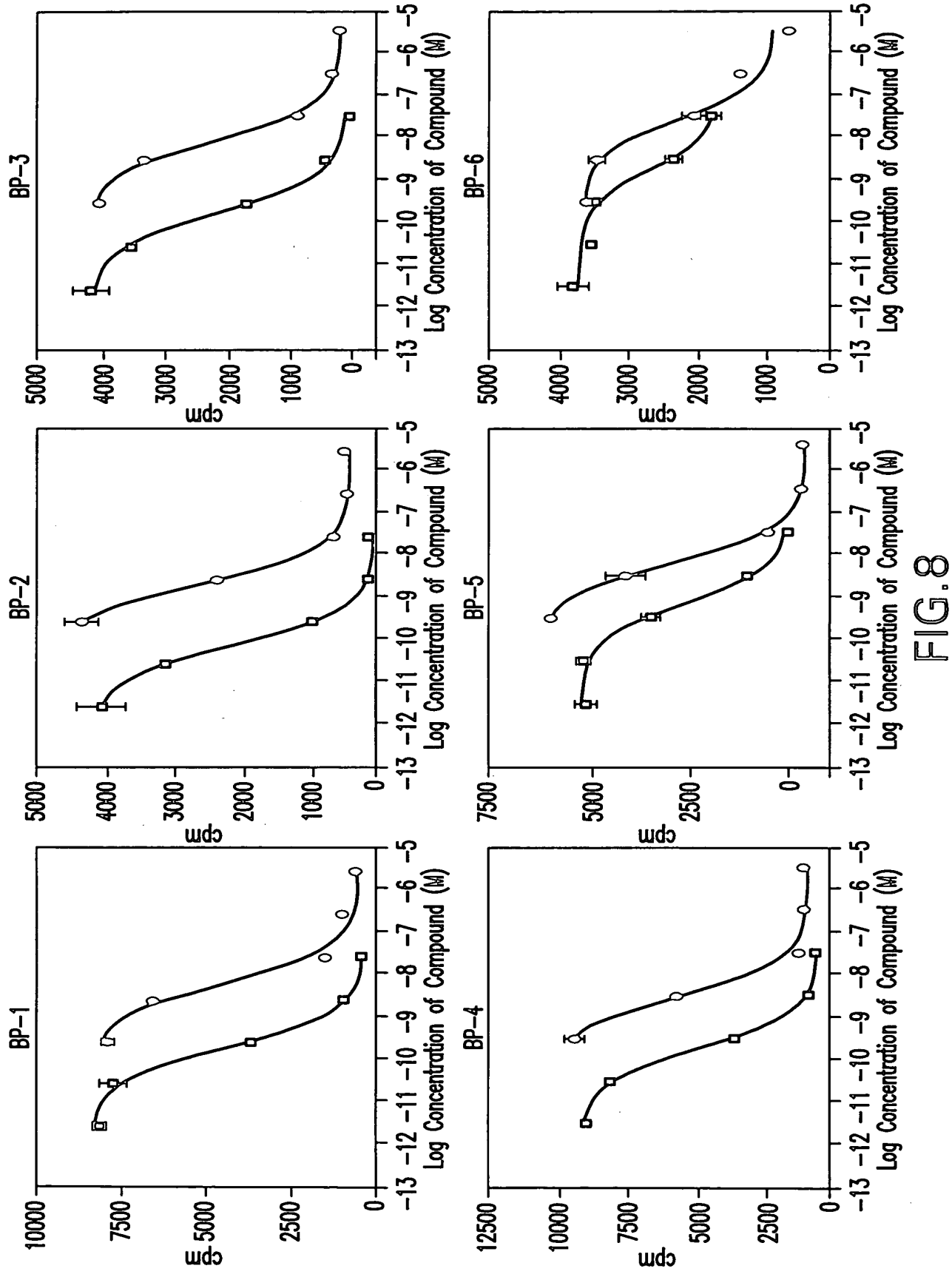
BP-1
BP-2
BP-3
BP-4
BP-5
BP-6
cpm
Log Concentration of Compound (M)
-13 -12 -11 -10 -9 -8 -7 -6 -5
0
2500
5000
7500
10000
12500
1000
2000
3000
4000

FIG. 8

```
                1                                                   50
IGFBP3_prote ~~~~~MORAR PTLWAAALTL LVLLRGPPVA RAGASSGGLG PVVRCEPCDA
IGFBP5_prote ~~~~~~~~~~ ~~~~MVLLTA VLLLL...AA YAGPAQ.SLG SFVHCEPCDE
IGFBP2_prote MLPVVGCPAL PLPPPPLLPL LPLLLLLLGA SGGGGGARAE VLFRCPPCTP
IGFBP4_prote ~~~~~~~~~~ ~~~~~~MLPL CLVAALLLAA ..GPGPSLGD EAIHCPPCSE
IGFBP1_prote ~~~~~~~~~~ ~~~~~~MLPL CLVAALLLAA ..GPGPSLGP EAIHCPPCSE
IGFBP6_prote ~~~~~~~~~~ ~~MSEVPVAR VWLVLLLLTV QVG...VTAG APWQCAPCSA
IGFBP7_prote ~~~~~~~~~~ MTPHRLLPPL LLLLALLLAA SPG......G ALARCPGCGQ

                51                                                  100
IGFBP3_prote RALAQCAPPP .......... .....AVCAE LVREPGCGCC LTCALSEGQP
IGFBP5_prote KALSMCPPSP .......... .....LGC.E LVKEPGCGCC MTCALAEGQS
IGFBP2_prote ERLAACGPPP VAPPAAVAAV AGGARMPCAE LVREPGCGCC SVCARLEGEA
IGFBP4_prote EKLARCRPP. .......... .....VGCEE LVREAGCGCC ATCALGLGMP
IGFBP1_prote EKLALCPP.. .......... ...VSASCSE VTRSAGCGCC PMCALPLGAA
IGFBP6_prote GVQAGCP... ..GGCVEEED GGSPAEGCAE ...AEG.... ..CLRREGQE
IGFBP7_prote ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~

                101                                                 150
IGFBP3_prote CGIYTERCGS GLRCQPSPDE ARPLQALLDG RGLCVNASAV SRLRAYLLPA
IGFBP5_prote CGVYTERCAQ GLRCLPRQDE EKPLHALLHG RGVCLNE... ...KSY....
IGFBP2_prote CGVYTPRCGQ GLRCYPHPGS ELPLQALVMG EGTCEKRRDA EYG...ASPE
IGFBP4_prote CGVYTPRCGS GLRCYPPRGV EKPLHTLMHG QGVCMEL..A EIE...AIQE
IGFBP1_prote CGVATARCAR GLSCRALPGE QQPLHALTRG QGACVQESDA SAPHAAEAGS
IGFBP6_prote CGVYTPNCAP GLQCKPPKDD EAPLRALLLG RGRCLPAR.. ..........
IGFBP7_prote ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~
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FIG.9A

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                151                                                 200
IGFBP3_prote PPAPGNASES EEDRSAGSVE SPSVSS.THR VSDPK.FKPL HSKIIIIKKG
IGFBP5_prote ......REQV KIERDSREHE EPTTSEMAEE TYSPKIFRPK HTRISELKAE
IGFBP2_prote QVADMGDDHS EGGLVENHVD STMNMLGGGG SAGRKPLKSG MKELAVF...
IGFBP4_prote SLQPS..DKD EG.......D HPNNSFSPCS AHDRRCLQ.. .KHFAKI...
IGFBP1_prote PESPESTEIT EEELLDNFH. .....LMAPS EEDHSILWDA ISTYDGSKAL
IGFBP6_prote ..APAVAE.. .........E NPKESKPQAG TA........ ..........
IGFBP7_prote ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~

                201                                                 250

IGFBP3_prote HAKDSQRYKV DYSEQSTDTQ N.......FS SESKRETEYG PCRREMEDTL
IGFBP5_prote AVKKDRRKKL TQSKFVGGAE NTAHPRIISA PEMRQESEQG PCRRHMEASL
IGFBP2_prote ......REKV TEQHRQMGKG GKHHLGLEEP KKLRPPPART PCQQELDQVL
IGFBP4_prote ......RPRS T.......SG GKMKVNGAPR EDARPVP.QG SCQSELHRAL
IGFBP1_prote HVTNIKKWK. .......... .......... .........E PCRIELYRVV
IGFBP6_prote ......RPQD VNRRDQQRNP GTSTTPSQPN SAGVQPTEMG PCRRHLDSVL
IGFBP7_prote ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~

                251                                                 300
IGFBP3_prote NHLKFLNVLS PRA.......  VHIPNCDKKG FYKKKQCRPS KGRKRGFCWC
IGFBP5_prote QELKASPRMV PRA.......  VYLPNCDRKG FYKRKQCKPS RGRKRGICWC
IGFBP2_prote ERISTMRLPD ERGPLEHLYS LHIPNCDKHG LYNLKQCKMS LNGQRGECWC
IGFBP4_prote ERLAA....S QSRTHEDLYF IPIPNCDRNG NFHPKQCHPA LDGQRGKCWC
IGFBP1_prote ESLA....KA QETSGEEISK FYLPNCNKNG FYHSRQCETS MDGEAGLCWC
IGFBP6_prote QQL....... QTEVYRGAQT LVVPNCDHRG FYRKRQCRSS QGQRRGPCWC
IGFBP7_prote ~~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~~~~~~~~~~~ ~~~~~~~~~~
```

FIG.9B

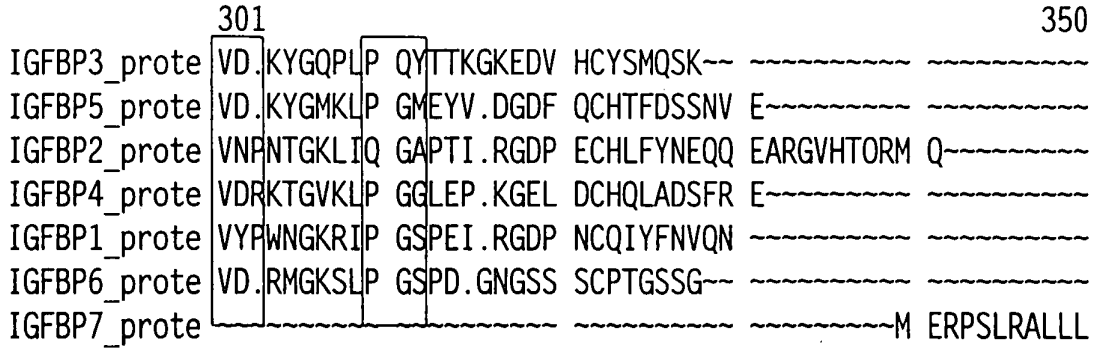

FIG.9C

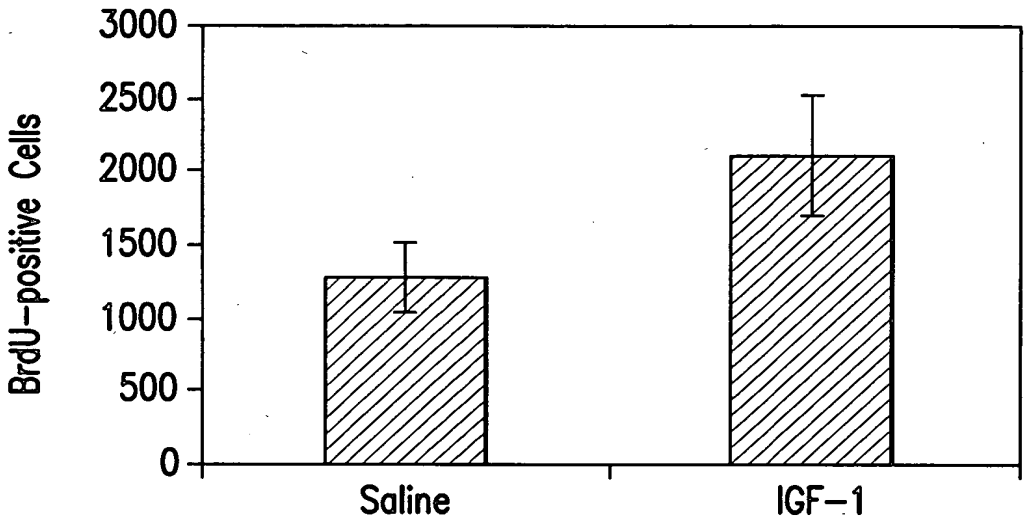
BrdU-positive Cells
3000
2500
2000
1500
1000
500
0
Saline
IGF-1

FIG. 10